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A new lung donor score to predict short and long-term survival in lung transplantation

Ehram, Jonas P ; Held, Ulrike ; Opitz, Isabelle ; Inci, Ilhan

Abstract: Background Donor selection criteria are crucial for a successful lung transplant outcome. Our objective was to develop a new donor score to predict short- and long-term survival and validate it with five existing lung donor scores (Oto, Eurotransplant, Minnesota, Maryland-UNOS, Louisville-UNOS). **Methods** All 454 adult lung transplants at our center between 1992-2015 were included to develop a new score. Discriminative ability for all scores was calculated by the area under time-dependent receiver operating characteristic curves (time-dependent AUC) at 30-day, 1, 5 and 10-year survival, and their fit compared with Akaike's information criterion. For the new score, five pre-selected donor risk factors were derived: age, diabetes mellitus, smoking history, pulmonary infection, PaO₂/FiO₂-ratio, weighed via simplification of a multiple Cox model, and shrinkage used to avoid overfitting. The score sub-weighting resulted in a total of 17 points. **Results** The existing scores showed predictive accuracy better than chance in prediction of survival of 5-year (AUC 0.58-0.60) to 10-year survival (AUC 0.58-0.64). Our new score had better discriminative ability as the existing scores with regard to 1, 5 and 10-year survival (AUC 0.59, 0.64, 0.66, respectively). Additional adjustment for recipient and surgical procedure variables improved the time-dependent AUC's slightly. For the secondary outcomes primary graft dysfunction and bronchiolitis obliterans syndrome, the new score showed also a good predictive accuracy. **Conclusions** The proposed Zurich Donor Score is simple, well adapted for the current urge of extended donors use, and shows higher discriminative ability compared to preexisting donor scores regarding short- to long-term survival.

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A new lung donor score to predict short and long-term survival in lung transplantation

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Background: Donor selection criteria are crucial for a successful lung transplant outcome. Our objective was to develop a new donor score to predict short- and long-term survival and validate it with five existing lung donor scores (Oto, Eurotransplant, Minnesota, Maryland-UNOS, Louisville-UNOS).

Methods: All 454 adult lung transplants at our center between 1992–2015 were included to develop a new score. Discriminative ability for all scores was calculated by the area under time-dependent receiver operating characteristic curves (time-dependent AUC) at 30-day, 1, 5 and 10-year survival, and their fit compared with Akaike's information criterion. For the new score, five pre-selected donor risk factors were derived: age, diabetes mellitus, smoking history, pulmonary infection, PaO₂/FiO₂-ratio, weighed via simplification of a multiple Cox model, and shrinkage used to avoid overfitting. The score sub-weighting resulted in a total of 17 points.

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Conclusions: The proposed Zurich Donor Score is simple, well adapted for the current urge of extended donors use, and shows higher discriminative ability compared to preexisting donor scores regarding short- to long-term survival.

Keywords: Lung transplantation; lung allocation; lung donor score; extended criteria donor; primary graft dysfunction; bronchiolitis obliterans syndrome

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Introduction

Organ shortage and a growing demand for lung transplantations force several centers to increasingly use extended donor lungs. In 2003 the International Society for Heart and Lung Transplantation (ISHLT) released a consensus report (1) defining an ideal donor lung based

on 5 variables: age <55, smoking history <20 pack years, uncompromised chest X-ray, clear bronchoscopy and pulmonary arterial oxygen tension/fraction of inspired oxygen-ratio >300 mmHg.

In the meantime, several attempts were made to further specify and identify potential extended criteria. In 2007 Oto

et al. (2) at the University of Melbourne suggested a score based on the ISHLT-criteria to predict donor selection and early post-lung-transplant outcome. In 2011 the Oto-Score was modified by the European allocation organization Eurotransplant (3) to a new score serving the same purpose. In 2016 the University of Minnesota (4) created a new, complex, consensus-based lung scoring system to predict lung offer acceptance and usability for transplantation. However, the University of Maryland (5) identified donor risk factors based on United Network for Organ Sharing (UNOS) data and created a single point score that was associated with one-year survival, based on just four simple risk factors. Lately, the University of Louisville (6) identified almost identical four risk factors in the same data base and showed an association with 1 and 5-year survival.

To date, only the Oto-Donor-Score has been externally validated with inconsistent results (4,7). Except for the Louisville-UNOS donor score, nothing is known about the utility of any of these scores to predict long-term survival.

The goal of the current study was first, to validate the short- and long-term predictive ability of five published scores based on our centers transplant pool and second, to develop a new and simple donor score for survival that includes donor parameters prior to procurement. We present the following article in accordance with the TRIPOD reporting checklist (available at <http://dx.doi.org/10.21037/jtd-20-2043>).

Methods

We performed a retrospective study of all adult recipients and their corresponding donors transplanted at the University Hospital of Zurich between 11/1992 and 12/2015, with last follow-up in 10/2019. Donor and recipient data were collected retrospectively from prospectively entered medical records. For donor variables, the values at the time of donor acceptance, prior to procurement were used. Infection suspected on radiological findings in the contralateral lung were ignored in cases where only unilateral transplants were performed. The collected donor variables were compared to findings in the donor report at the time of procurement. The study has been approved by the Cantonal Ethics Committee Zurich (KEK-ZH-Nr.2013-0624), and the need to obtain informed consent was waived because of the retrospective observational nature of the study. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Outcomes

The primary outcome was survival after lung transplantation. Secondary outcomes were primary graft dysfunction grade 3 (PGD3) (8), defined as $\text{PaO}_2/\text{FiO}_2$ -ratio <200 mmHg and the presence of diffuse parenchymal infiltrates in the allograft on chest radiograph at 72 hours after transplantation (binary outcome); as well as severe bronchiolitis obliterans syndrome grade III (BOS-III) (9), defined as a persistent decline of forced expiratory volume in 1 second (FEV1) $\leq 50\%$ and an obstructive physiology (time-to-event).

Definition of predictor variables

Variables of the existing donor scores

The variables of the five existing donor scores are shown in *Tables S1-S5*. Oto-Score (2) consists of 5 subdivided donor criteria based on the ISHLT-Consensus Report (1). Eurotransplant-Score (3) is a simplified version of Oto-Score with the addition of a compromised history. The University of Minnesota-Donor-Lung quality index (4) includes 17 subdivided factors of which one factor represents the recipient specific American Lung Allocation Score (LAS). As LAS is not used in Switzerland, we excluded LAS for this score but adjusted for recipient and surgical procedure variables subsequently. To make the results of the evaluation of the Minnesota score comparable to the results of the other scores, the scale was reversed such that higher values are associated with higher risk for mortality. University of Maryland-UNOS-data donor score (5) and Louisville-UNOS-data score (6) are very simple scores based on the same 4 variables, except that the later uses different breaks for age.

Development of the Zurich-Donor-Score for prediction of mortality

A larger and preliminary set of potential risk variables was defined consisting of all variables of the five existing donor scores (*Tables S1-S5*) and availability. A preselection of variables was performed according to the estimated hazard ratios (HR) and P values from univariate Cox regression models with outcome survival. If the corresponding HR was ≥ 1.2 and P value < 0.2 , the predictor variable was assumed to be relevant for risk prediction (10). The final set of variables used to develop the new donor score included the following variables: significant pulmonary infection, diabetes mellitus, $\text{PaO}_2/\text{FiO}_2$ -ratio, smoking history in pack

years, and donor age. The three continuous variables were categorized by the study team according to multiple non-linear graphical assessment using splines and consideration of the recent literature. After categorization of the continuous variables, all variables were coded as factor variables and their association with survival was assessed in a multiple Cox model. Resulting estimated beta-coefficients were shrunk globally to account for overfitting. Shrinkage is a statistical technique used in regression analysis, to avoid overfitting (11). Subsequently, the new score's values were assigned following the rule that estimated beta-coefficients of 0.1 to 0.2 were assigned two points, such of 0.3 three points, such of 0.4 four points, and higher beta-coefficients five points. Score points were assigned in monotonous fashion with increasing category of risk factor.

Definition of recipient- and surgical procedure variables

To consider the impact of recipient and surgical procedure variables on post-transplant survival, we adjusted our models for the following risk factors that are well known from the literature and also present in our cohort: unilateral transplantation (12), retransplantation (12), idiopathic pulmonary fibrosis as underlying disease (12), preoperative intensive care unit stay (12), recipient age (12), and for the comorbidity profile the age independent Charlson-Deyo Index (13). No additional impact was observed by adjusting for up to 3 different transplant eras.

Statistical methods

Kaplan-Meier method was used to estimate survival as well as time to development of BOS-III.

To estimate short and long-term predictive accuracy for each score, time dependent receiver operating characteristic curves (ROC) were applied, accounting for the fact that censoring was present. The time points shown in figures were 1 month, and 1, 5 and 10 years after transplantation. Areas under the ROC curves (AUC) were estimated at each of the pre-specified time points. To compare models' goodness of fit, Akaike's information criterion (AIC) was used, with lower AIC indicating better model fit. The AIC can be interpreted in such a way that a reduction of more than 2 points in the comparison of nested models would indicate a significantly better model fit, corresponding to a likelihood-ratio test.

For the development of a new score, multiple Cox proportional hazards models were used. The number of

predictors allowed to be simultaneously in the multiple Cox models was based on the number of events (deaths). The general rule of ten events per variable in the prediction model was considered (14). To address the problem of overfitting, the estimated coefficients of the Cox model were shrunk globally, with a shrinkage factor estimated with the DFBETA method (15). In this context, global shrinkage means that the same amount of shrinkage was applied to all estimated parameters. The assessment of the shrinkage factor with the DFBETA method corresponds to leave-one-out cross-validation (LOOCV) but is computationally more efficient. This aspect is of relevance especially when the number of observations is large as in this study (16). The closer the shrinkage factor to 1, the less shrinkage is required and the less overfitting was determined. The Cox proportional hazards (PH) assumption was evaluated with a score test based on Schoenfeld residuals. In case that the proportional hazards assumption for a variable was violated, a suitable cut-off for the variable was derived, and the proportional hazards assumption was re-evaluated.

For secondary outcomes, BOS-III was addressed with a Cox model in which non-survivors were censored, and the binary outcome PGD3 was addressed with a logistic regression model. All estimated coefficients were shown with 95% confidence intervals. All analyses were carried out with the statistical programming language R [R Core Team (2019)], version 3.6.0, and time-dependent ROC curves were fitted with the R-package "timeROC". Shrinkage was performed with R-package "shrink".

The results of this study were presented in accordance with the TRIPOD guidelines (17) for reporting of clinical prediction models.

Results

In our cohort, there were 454 adult recipients with lung transplantation between 1991 and 2015, and with at least 4 years follow-up. Of these, 320 recipients (70.5%) died. Median follow-up time was 14.2 years (95% confidence interval 12.4 to 16.0 years). No loss to follow-up occurred. Detailed descriptive statistics of recipient-, donor-, intra- and post-operative characteristics are shown in *Table 1*. More than 72% of all donors were non-ideal donors according to ISHLT consensus criteria (1) (*Table 1*).

Validation of the five existing donor scores in our cohort

Factors for Oto-Donor-Score (2), Eurotransplant-Score (3),

Table 1 Baseline recipient, donor, peri and post-operative

Characteristics	Outcome
Recipient characteristics	
N	454
Age (years), median (range)	48 (16–70)
Male gender	232 (51.1%)
Diagnosis (all)	
CF	147 (32.4%)
EMP	132 (29.1%)
PPH	27 (5.9%)
IPF	90 (19.8%)
Other	58 (12.8%)
ICU admission pre-operative	43 (9.5%)
mPAP >25 mmHg	235 (51.8%)
Waitlist time (days), median (range)	150 (0–1,965)
Charlson-Deyo Comorbidity index (12), median (range)	1 (0–4)
2	125 (27.5%)
3	45 (9.9%)
4	16 (3.5%)
5	3 (0.7%)
Donor characteristics	
Age (years), median (range)	45 (11–85)
Charlson-Deyo index (12), median (range)	0 (0–5)
1	42 (9.3%)
2	7 (1.5%)
3	5 (1.1%)
4	5 (1.1%)
5	1 (0.2%)
Cause of death	
Cranial bleeding/ischemia	
Traumatic	165 (36.3%)
Atraumatic	230 (50.7%)
Asphyxiation	51 (11.2%)
Other	8 (1.8%)
CMV mismatch	122 (26.9%)

Table 1 (continued)**Table 1** (continued)

Characteristics	Outcome
Extended criteria according to ISHLT (1)	
Age ≥55 years	128 (28.2%)
Smoking history ≥20 packyears	77 (17.0%)
Chest X-Ray pathologic	122 (26.9%)
Bronchoscopy pathologic	50 (11.0%)
PaO ₂ -FiO Ratio <300 mmHg	171 (37.7%)
Number, median (range)	1 (0–4)
1	161 (35.5%)
2	123 (27.1%)
3	39 (8.6%)
4	6 (1.3%)
Peri and post-operative characteristics	
Unilateral transplantation	36 (7.9%)
Retransplantation	19 (4.2%)
ECMO use	186 (41.0%)
Donor cardiac after circulatory death	16 (3.5%)
Max. ischemic time (minutes), median (range)	334 (132–885)
ICU time (days), median (range)	4 (1–311)
PGD Grade3 at 72 hours	75 (16.5%)

PGD, primary graft dysfunction; CMV, Cytomegalovirus; ICU, intensive care unit; ECMO, extracorporeal membrane oxygenation; mPAP, mean pulmonary artery pressure; CF, cystic fibrosis; IPF, interstitial pulmonary fibrosis; PPH, primary pulmonary hypertension; EMP, emphysema.

Minnesota-Donor-Lung quality index (4), Maryland-UNOS-data donor score (5) and Louisville-UNOS-data donor score (6) are illustrated in *Tables S1–S5*, respectively.

Akaike's information criterion revealed best model fit for predictability for Maryland-UNOS-data donor score with an AIC value of 3,414.4, followed by lower fit for Louisville-UNOS-data donor score (AIC 3,414.9), Minnesota-Donor-Lung quality index (AIC 3,417.8), Oto-Donor-Score (AIC 3,425.1) and finally the lowest fit for Eurotransplant-Score (AIC 3,426.3).

Development of the Zurich-Donor-Score

A multiple Cox model was used to evaluate the weight of

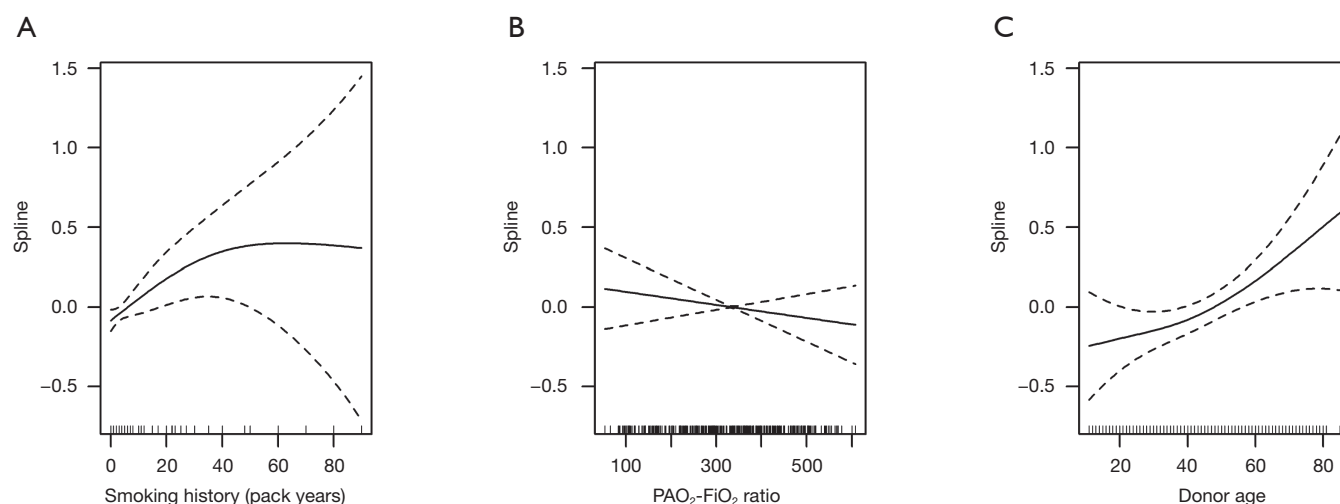


Figure 1 Additive non-linear effects using splines of the continuous variables in multiple Cox regression models. (A) Smoking history, (B) PAO₂/FiO₂-ratio and (C) donor age.

significant pulmonary infection, diabetes mellitus, PAO₂/FiO₂-ratio (in categories with breaks at 300 and 150 mmHg), smoking history (in categories with breaks at 20 and 50 pack years), and donor age (with breaks at 50 and 70 years). The breaks in the continuous variables were justified from fitting multiple non-linear Cox models using splines (*Figure 1*) and by the literature. After the multiple Cox model was fitted based on the categorical variables, there was some indication for overfitting, resulting in a global estimated shrinkage factor of 0.82. The new score varied between 0 (low mortality risk) and 12 (high mortality risk) in our sample, whereas mean and median of the new score were 3.3 and 3. Details can be found in *Table 2*. *Figure 2A* and *Table 3* show the results of a time-dependent ROC analysis of the new Zurich-Donor-Score as compared to the existing donor scores. The AIC value of the Zurich-Donor-Score was 3,398.9, which was lower than those of all existing donor score, indicating better model fit.

Assessing the predictive accuracy of all donor scores while adjusting for recipient and surgical procedure variables

Recipient and surgical procedure variables included unilateral transplantation, retransplantation, idiopathic pulmonary fibrosis as underlying disease, preoperative intensive care unit stay, recipient age, and age independent Charlson-Deyo Index. *Figure 2B* showed that recipient and surgical procedure variables are crucial in order to make predictions of survival over time. After one month,

donor and receiver information seem to be almost equally important, but as time passes, recipient and surgical procedure information from baseline become more important, leading to a substantially improved AUC for all scores at 10 years follow-up time. In a multiple Cox model with adjustment for recipient and surgical procedure variables, the estimated hazard ratio for the new score was 1.14 (95% CI: 1.09 to 1.19, $P < 0.001$) per point increase.

Secondary outcomes: time to BOS-III and PGD3

Although the new donor score was originally developed for the short- and long-term prediction of mortality after lung transplantation, the score may also be evaluated for the secondary outcomes BOS-III and PGD3. BOS-III was developed by 168 (37%) of the recipients. In a multiple Cox model with adjustment for recipient and surgical procedure variables, the estimated hazard ratio for the new score was 1.14 (95% CI: 1.07 to 1.21, $P < 0.001$) per point increase. Seventy-five percent recipients (17%) experienced PGD3. When the new score was evaluated in a multiple logistic regression model with PGD3 as outcome, again adjusting for recipient and surgical procedure variables, the estimated odds ratio was 1.13 (95% CI: 1.03 to 1.23, $P = 0.01$).

Discussion

Our study validates five existing donor scores in terms of short- and long-term survival, which were originally

Table 2 Development of Zurich Donor Score based on estimated β -coefficients from multiple Cox model and shrunk coefficients

Predictor	N	HR (95% CI)	β	Shrunk β	Score points Zurich donor score (total 17 points)
Significant pulmonary infection*					
Yes	127	1.46 (1.14–1.87)	0.38	0.31	3
No	327	–	–	–	0
Diabetes mellitus					
Yes	25	1.29 (0.80–2.10)	0.25	0.21	2
No	429	–	–	–	0
PaO ₂ /FiO ₂ -ratio (mmHg)					
>300	278	–	–	–	0
300 to >150	134	1.30 (1.01–1.66)	0.26	0.21	2
≤150	42	1.50 (1.22–1.87)	0.4	0.33	3
Smoking history (pack years)					
<20	377	–	–	–	0
20 to <50	69	1.43 (0.60–3.50)	0.36	0.29	3
≥50	8	1.63 (1.22–2.18)	0.49	0.4	4
Age (years)					
<50	273	–	–	–	0
50 to <70	151	1.31 (1.02–1.68)	0.27	0.22	2
≥70	30	2.24 (1.44–3.50)	0.81	0.66	5

β , β -coefficient; CI, confidence interval; HR, hazard ratio. *Radiological suspicion of pneumonia, bronchoscopic sign of severe bronchitis, history of aspiration (radiological suspicion of pneumonia: opacity in one or more lobes not predominantly resembling in morphology to atelectasis or edema; Signs of severe bronchitis: purulent secretions and/or signs of bronchial inflammation in bronchoscopy; History of aspiration: observed aspiration, signs in bronchoscopy of aspiration or a history highly suspicious of aspiration).

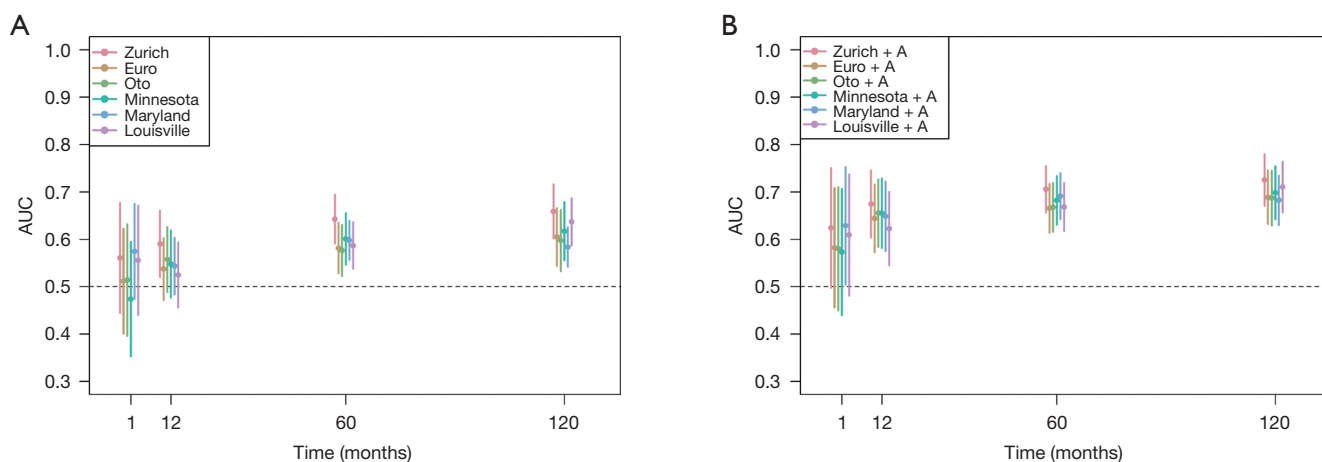


Figure 2 Time dependent AUC values for the five existing donor scores and the new Zurich-Donor-Score. (A) Unadjusted, based on donor information alone; (B) adjusted for recipient and surgical procedure variables. A = adjustment for recipient and surgical procedure variables.

Table 3 Time dependent AUC values based on donor information alone

	AUC	SE
Zurich Donor Score		
30 days	0.56	0.06
1 year	0.59	0.04
5 years	0.64	0.03
10 years	0.66	0.03
Eurotransplant Score (3)		
30 days	0.51	0.06
1 year	0.54	0.03
5 years	0.58	0.03
10 years	0.61	0.03
Oto Donor Score (2)		
30 days	0.51	0.06
1 year	0.56	0.04
5 years	0.58	0.03
10 years	0.6	0.03
Minnesota-Donor-Lung quality index (4)		
30 days	0.47	0.06
1 year	0.55	0.04
5 years	0.6	0.03
10 years	0.62	0.03
Maryland-UNOS-data donor score (5)		
30 days	0.58	0.05
1 year	0.54	0.03
5 years	0.6	0.02
10 years	0.58	0.02
Louisville-UNOS-data donor score (6)		
30 days	0.56	0.06
1 year	0.53	0.04
5 years	0.59	0.03
10 years	0.64	0.03

AUC, area under the ROC curve; SE, standard error.

developed to simplify donor selection and to predict short- to mid-term survival. In addition, we propose a new and simple scoring system that is well adapted for the current urge of extended donor use and shows higher discriminative

ability for short- to long-term survival.

Our transplant center in Switzerland has long-term experience in utilizing extended criteria donor lungs (18). The recent lung acceptance rate of 46% is higher than in most other European centers and the United States, but the long-term survival results are comparable (19). More than 70% of all recipients in our study received a not ideal donor lung based on the ISHLT-consensus criteria (1), offering good conditions for validation of existing donor scores and the derivation of a new scoring system.

Qualitative summary of the existing donor scores

The relatively complex donor scoring systems of Oto (2), Eurotransplant (3) and Minnesota (4), which were originally created to predict donor selection, lead to a slightly poorer prediction of short- and long-term survival as did the simple Maryland-UNOS-data (5) and Louisville-UNOS-data score (6), which were derived to predict short-term survival and mid-term survival, respectively.

Qualitative summary of the Zurich-Donor-Score

For our new and simple extended donor prediction score, we identified and weighted five donor risk factors that are available at the time of donor selection: age (breaks at ≥ 50 and ≥ 70 years), smoking history (breaks at ≥ 20 and ≥ 50 pack years), significant pulmonary infection, insulin dependent diabetes mellitus and $\text{PaO}_2/\text{FiO}_2$ -ratio (breaks at ≤ 300 and ≤ 150 mmHg).

Increasing donor age has an increasing negative impact on survival according to our findings which is comparable with the recent ISHLT-Registry Report (12). Our lower break of 50 or more years fits the start of risk of a large study using the UNOS-Database (20).

The observed increasing risk with increasing donor smoking history fits the idea of the donor scoring systems of Oto (2). The lower break of 20 or more pack years is in agreement with the ISHLT-consensus criteria (1) and a recent study using UNOS-Data (4).

Our risk factor of a significant pulmonary infection includes radiological findings suspicious of pneumonia, bronchoscopic signs of severe bronchitis and history of aspiration. These were defined as extended criteria according to ISHLT-consensus report (1). We combined and reduced these criteria, as their impact is to a certain extent controversial. Some studies have pointed out that lungs with radiological hints of pulmonary infiltrates did

not affect transplant survival (21,22). Other studies showed that radiological abnormalities and additional purulent bronchoscope secretion (23) and radiological abnormalities and additional reduced gas exchange (18) did increase mortality.

Donor diabetes mellitus is a widely accepted (5,12) risk factor, even though the pathophysiology is not yet clearly known (24).

Our detected risk of a declining $\text{PaO}_2/\text{FiO}_2$ -ratio from 300 mmHg downwards fits the recommendation of the ISHLT-consensus criteria (1). While a multicenter study found an impact (25), data from UNOS (26) suggest partial pressure of oxygen levels of lower than 200 mmHg do not affect graft survival. That's why we weighted this factor proportionally low in our score.

Our final Zurich-Donor-Score showed better prediction of 1 to 10-year survival in comparison to the five existing scores.

Although this new donor score was originally developed for the short- and long-term prediction of mortality after lung transplantation, the score also showed predictability for development of BOS-III and PGD3. This may be explained to a certain extent by the incorporated risk factors of age and smoking history. Older age was identified as a risk factor for BOS-III in some studies (27,28), while it is still controversial in causing PGD3 (29,30). Any donor smoking was reported to have an association with BOS-III (27) and a negative impact on PGD3 (31). The significance of donor lung infection for PGD3 is not yet understood (32).

Limitations and strengths

This study has several limitations. It is a retrospective single-center study over more than two decades, however without an era effect in univariable and multiple analyses, even though we stratified in different models up to 3 eras. All donor variables and subsequent calculation of scores are based on pre-procurement parameters. Although we did not find any discrepancies between these values and the donor lung reports at the time of retrieval, the values might not account for exact results of the physical examination of the lung at the time of retrieval (33). We acknowledge that variables such as the interpretations of chest X-ray and bronchoscopy are to some extent subjective. As our data collection is limited, there might have been some other important donor variables, which were not found to be important, because their prevalence was low in our setting. For example, we were not able to include data from the

African race, a variable which is part of the Maryland- and Louisville-UNOS-data donor score. We also acknowledge that performance of the original Minnesota-Donor-Lung quality index including LAS might have been superior to our compensative adjustment for recipient and surgical procedure variables. Our study has several strengths: we used shrinkage of estimated coefficients prior to the development of the new score, a method to reduce overfitting that would otherwise lead to low predictive performance in new data sets. Consequently, this approach of shrinkage manages to already preclude optimism of the score without the need of a separate validation cohort.

Conclusions

The proposed Zurich-Donor-Score is a simple scoring system of five objective and easily available pre-procurement donor variables. The new score shows higher discriminative ability when compared to existing donor scores regarding short- to long-term survival. This score is not yet evaluated for organ acceptance; this is currently being studied. In the reality of severe organ shortage and urge for more extended grafts, our proposed new score may be useful for clinical decision making in donor selection, allocation to specific recipient populations, comparison of data across centers, and thereby maximize the donor pool.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/jtd-20-2043>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved. The study has been approved by the Cantonal Ethics Committee Zurich (KEK-ZH-Nr. 2013-0624), and the need to obtain informed consent was waived because of the retrospective observational nature of the study. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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Supplementary

Table S1 Oto-Donor-Score (2)

	Points (total 18 points)	Cohort (N=454)	Univariable Cox regression	
			HR; 95% CI	P value
Age (years)				
<45	0	221 (48.7%)	–	
45–54	1	105 (23.1%)	1.1; 0.8–1.4	0.5
55–59	2	48 (10.6%)	1.4; 1.0–2.0	0.05
≥60	3	80 (17.6%)	1.5; 1.1–1.9	0.01
Smoking history (pack-years)				
<20	0	377 (83.0%)	–	
20–39	1	56 (12.3%)	1.6; 1.2–2.2	0.002
40–59	2	16 (3.5%)	1.7; 1.0–2.9	0.06
≥60	3	5 (1.1%)	–	
Chest X-ray				
Clear	0	245 (54.0%)	–	
Minor	1	90 (19.8%)	0.9; 0.8–1.2	0.6
Opacity ≤1 lobe	2	64 (14.1%)	1.0; 0.8–1.3	0.7
Opacity >1 lobe	3	55 (12.1%)	1.0; 0.7–1.4	0.9
Secretions in bronchoscopy				
None	0	384 (84.6%)	–	
Minor	1	23 (5.1%)	1.2; 0.9–1.7	0.2
Moderate	2	17 (3.7%)	1.2; 0.8–1.8	0.3
Major	3	30 (6.6%)	1.7; 1.1–2.7	0.02
PaO ₂ /FiO ₂ (mmHg)				
>450	0	90 (19.8%)	–	
351–450	2	139 (30.6%)	0.9; 0.7–1.2	0.7
301–350	4	55 (12.1%)	0.8; 0.6–1.2	0.4
≤300	6	170 (37.4%)	1.2; 1.0–1.5	0.08

CI, confidence interval; HR, hazard ratio.

Table S2 Eurotransplant-Score (3)

	Points (total 19 points)	cohort (N=454)	Univariable Cox regression	
			HR; 95% CI	P value
Age (years)				
<45 and 45–54	1	326 (71.8%)	–	
55–59	2	48 (10.6%)	1.4; 1.0–2.0	0.05
≥60	3	80 (17.6%)	1.5; 1.1–1.9	0.01
Smoking history (pack-years)				
Yes	2	277 (61.0%)	–	
No	1	177 (39.0%)	1.2; 1.0–1.6	0.06
Chest X-ray				
Clear, Edema or Atelectasis	1	335 (73.8%)	–	
Shadow or Consolidation	2	119 (26.2%)	1.0; 0.8–1.3	0.9
Secretions in bronchoscopy				
Clear or nonpurulent	1	405 (89.2%)	–	
Purulent	2	27 (5.9%)	1.1; 0.8–1.7	0.5
Inflammation	3	22 (4.8%)	1.6; 1.0–2.7	0.05
Visualized tumor	5	–	–	
PaO ₂ /FiO ₂ (mmHg)				
>450 and 351–450	1	216 (47.6%)	–	
301–350	2	68 (15.0%)	0.8; 0.6–1.2	0.4
≤300	3	170 (37.4%)	1.2; 1.0–1.5	0.08
Donor history				
Compromised*	4	28 (6.2%)	1.1; 0.9–1.2	0.4
Uncompromised	1	426 (93.8%)	–	

CI, confidence interval; HR, hazard ratio. *The donor history is compromised in case of malignancy, sepsis, drug abuse, meningitis, or a positive virology was registered

Table S3 Minnesota-Donor-Lung quality index (4)

	Points [possible range of points (0–48)]	Cohort (N=454)	Univariable Cox regression	
			HR; 95% CI	P value
1. Anticipated ischemic time				
<6 hours	1	404 (89.0%)	–	
≥6 hours	0	50 (11.0%)	1.0; 0.7–1.4	0.9
2. Risk of pneumonia				
Low	4	173 (38.1%)	–	
Moderate	2	232 (51.1%)	1.0; 0.8–1.2	0.9
High	0	49 (10.8%)	1.1; 1.0–1.1	0.2
3. Donor age				
15–45 years	2	234 (51.5%)	–	
46–65 years	1	178 (39.2%)	1.2; 0.9–1.5	0.1
>65 years	0	42 (9.3%)	1.9; 1.3–2.7	0.001
4. Risk of aspiration injury				
Low	3	411 (90.5%)	–	
Moderate	2	28 (6.2%)	1.2; 0.8–1.7	0.4
High	0	15 (3.3%)	1.4; 0.7–2.9	0.3
5. Risk of preexisting lung disease				
Low	4	446 (98.2%)	–	
Moderate	2	8 (1.8%)	1.0; 0.8–1.2	0.9
High	0	–	–	
6. Risk of pulmonary edema				
Low	3	447 (98.5%)	–	
Moderate	2	7 (1.5%)	1.7; 0.8–3.7	0.1
High	0	–	–	
7. Risk of contusion				
Low	2	428 (94.3%)	–	
Moderate	1	15 (3.3%)	0.7; 0.5–1.2	0.2
High	0	11 (2.4%)	1.0; 0.5–2.0	0.9
8. Blood gasses				
Good	3	284 (62.6%)	–	
Marginal	0	170 (37.4%)	0.9; 0.9–1.0	0.05
9. Smoking history				
<30 Pack-years	2	397 (87.4%)	–	
≥30 Pack-years	0	57 (12.8%)	1.7; 1.2–2.3	0.001
10. Anticipated procurement complexity				
Simple	2	415 (91.4%)	–	
Moderate	1	36 (7.9%)	1.0; 0.6–1.5	0.9
Complex	0	3 (0.7%)	–	
11. Risk of pulmonary malignancy				
Low	5	283 (62.3%)	–	
Moderate	4	94 (20.7%)	1.1; 0.8–1.4	0.7
High	0	77 (17.0%)	1.6; 1.2–2.1	0.001
12. Risk of donor-transmitted diseases				
Low	4	452 (99.6%)	–	
Moderate	3	2 (0.4%)	–	
High	0	–	–	
13. Risk of extrapulmonary malignancy				
Low	5	445 (98.0%)	–	
Moderate	2	9 (2.0%)	0.9; 0.7–1.1	0.2
High	0	–		
14. Risk of positive retrospective HLA crossmatch				
Low	5	454 (100%)	–	
Moderate	3	–		
High	0	–		
15. Risk of size mismatch				
Low	3	294 (64.8%)		
Moderate	2	23 (5.1%)	1.1; 0.9–1.4	0.3
High	0	137 (30.2%)	1.3; 1.0–1.6	0.06

CI, confidence interval; HLA, human leukocyte antigen; HR, hazard ratio.

Table S4 Maryland-UNOS-data donor score (5)

	Points (total 4 points)	Cohort (N=454)	Univariable Cox regression	
			HR; 95% CI	P value
Age ≥65 years	1	42 (9.3%)	1.9; 1.3–2.7	0.001
Smoking history ≥20 packyears	1	77 (17.0%)	1.7; 1.3–2.2	<0.001
Diabetes	1	25 (5.5%)	1.8; 1.1–2.9	0.01
African American race	1	–	–	

CI, confidence interval; HR, hazard ratio.

Table S5 Louisville-UNOS-data donor score (6)

	Points (total 5 points)	Cohort (N=454)	Univariable Cox regression	
			HR; 95% CI	P value
Age, years				
51–60	1	97 (21.4%)	1.3; 1.0–1.7	0.05
>60	2	71 (15.6%)	1.5; 1.5–2.1	0.005
Smoking history >20 packyears	1	77 (17.0%)	1.7; 1.3–2.2	<0.001
Diabetes	1	25 (5.5%)	1.8; 1.1–2.9	0.01
African American race	1	–	–	

CI, confidence interval; HR, hazard ratio.